REMARKS

By this Amendment, claims 30, 37, 38, 40, 41, 48, 55, 56, 59 and 60 are amended. Support for the amendments is found in the specification. No new matter is introduced.

Applicants and their representative thank Examiner Marvich for the productive telephonic interview held on May 13, 2008. The arguments presented below reflect the discussion during the interview.

Claim Objections

Applicants have amended claims 30 and 48 to clarify step d) as suggested by the Examiner. Applicants request that the Examiner clarify the objections with respect to claims 1 (cancelled), 38, 55 and 66, since the objected language does not appear in these claims. All remaining Examiner's suggestions for amending claims 38, 40, 41, 48, 55, 56, 59, and 60, are fully adopted.

§ 102 Rejection

Claims 30, 36, 37 and 40 have been rejected under § 102(b) and § 102(e) over US Patent No. 5,859,227 (the '227 patent). In the interview on May 13, the Examiner stated that the 102 (b) rejection should have been based on PCT publication WO 98/37422, instead of the '227 patent. It was agreed that both documents have an equivalent disclosure. Thus, if the § 102(e) rejection over the '227 patent is withdrawn because it does not disclose all elements of the invention, it follows that the § 102 (b) rejection over WO 98/37442 must also be withdrawn for the same reason. For ease of reference, both documents will be referred to here as *Giordano*, with specific cites referencing the '227 patent.

In rejecting the claims under § 102, the Examiner stated:

> Giordano et al teach methods of identifying interactions between RNA binding proteins and RNA molecules in bulk in lysates (see e.g. bridging ¶ col 4-5) and of compounds that affect these interactions (see e.g. col 5, line 9-10). The interactions are detected by detection of a label or use of an antibody to RBP (see e.g. col 5, line 9-10). [Office Action dated April 22, 2008, at page 4.]

Applicants respectfully disagree with this characterization of *Giordano* as explained in detail below.

A. Claims 30-38 and 40-47 (antibodies)

As discussed during the interview, *Giordano*, properly interpreted, does not disclose all elements of claim 30, and thus, cannot anticipate this claim or any of its dependent claims. Specifically, claim 30 is directed to a method wherein lysates are contacted with an antibody binding a component of mRNP complexes. Thereafter, resulting complexes are partitioned by capturing the antibody on a solid support, the lysates are then removed, and the complexes are analyzed to identify a plurality of RNAs.

Giordano uses a different approach. To start with, *Giordano*'s title is "RNA sequences which interact with RNA-binding proteins." As seen from the description of Figures 1-5 at cols. 3-4 and Examples 1-3, as well as other parts of this reference, *Giordano* utilizes certain RNA sequences – not antibodies – to form RNA-protein complexes from crude cellular or nuclear extracts. Nowhere does *Giordano* teach using antibodies for precipitating mRNA-protein complexes onto a solid support. Moreover, a word search in *Giordano* for the terms "antibody" or "antibodies" produces only four instances, all of which are found in the following two passages:

First Passage

> Detection of interactions between RNA binding proteins and RNA molecules can be facilitated by attaching a detectable label to the RNA binding protein. Generally, labels known to be useful for proteins can be used to label RNA binding proteins. Preferred labels for RNA binding proteins are ^{251}I, ^{3}H, and ^{35}S. When the RNA binding protein is made recombinantly, it can be labeled by incorporation of labeled amino acids. Techniques for labeling and detecting labeled proteins are well known and are described in, for example, Sambrook et al., and Ausubel et al., Current Protocols in Molecular Biology (John Wiley & Sons, Inc., 1996). Detection of RNA binding proteins can also be accomplished with ***antibodies*** specific for the RNA binding protein. The production and use of ***antibodies*** for this purpose is well known as is described in, for example, Johnstone and Thorpe, Immunochemistry in Practice (Blackwell Scientific Publications, 1987). [Col. 7, lines 53-59; emphasis added.]

Second Passage

> 6. Identifying Genes Encoding RNA binding Proteins
> The genes encoding RNA binding proteins that interact with RNA molecules can be identified by isolating the binding protein and determining a portion of the amino acid sequence. This sequence can then be used to generate peptides which in turn can be used to produce ***antibodies*** to the RNA binding

> protein. Additionally, or alternatively, the peptide sequence can be reverse translated to generate a cDNA probe. The probes or ***antibodies*** can then be used to screen a cDNA library (expression library when antibodies are used) and resulting cDNA clones used to screen a genomic library. [Col. 16, line 60, to col. 17, line 5; emphasis added.]

The second passage refers to *screening an expression library*. This process does not entail partitioning and analysis of mRNA-protein complexes as recited by claim 30.

As for the first passage, it would be readily understood by one of skill in the art, that it relates to *detection* of RNA binding proteins in RNA-protein complexes *that have already been isolated* from lysates. In fact, all specific examples of detection methods in *Giordano* include isolation of complexes prior to detection of their components. These specific examples include a) filter binding, b) gel mobility shift, and c) ribonuclease digestion. (See, e.g., col. 14, lines 10-21 et seq. "It is preferred that detection involve separation of interacting RNA molecules and RNA[,] binding proteins. ... The preferred methods ... are filter binding and gel mobility shift...") Furthermore, *Giordano* also describes the use detectable labels (e.g., radioactive labels) for "detection" in the same paragraph where it mentions the use of antibodies for the same purpose. Col. 7, lines 53-59. In other words, *Giordano* teaches using both, radioactive labels or antibodies, for the same purpose, which is discerning the presence or identity of components in the *isolated* RNA-protein complexes. *Giordano* does *not* teach using antibodies for "partitioning," "isolation," and/or "precipitation" of mRNA-protein complexes. Therefore, *Giordano* does not disclose all elements of claim 30, and in particular, it does not disclose "*partitioning the mRNP complex by capturing an antibody on a solid support.*" Accordingly, the § 102 rejection of claim 30 and its dependent claims should be withdrawn.

B. Claims 48-67 (epitope-tagged RBPs or RAPs)

Giordano does not disclose all of the elements of claim 48, and therefore, cannot anticipate this claim or any of it dependent claims. Claim 48 calls for expressing an epitope-tagged RNA-binding protein (RBP) or an epitope-tagged RNA-associated protein (RAP) in cells. The cells, expressing such proteins, are lysed, and the complexes are partitioned by capturing the endogenously expressed epitope-tagged protein onto a solid support. Thereupon, the lysates are removed, and the complexes are analyzed to identify a plurality of RNAs.

As discussed above, *Giordano* utilizes certain RNA sequences – not epitope-tagged RBPs or RAPs – to form RNA-protein complexes from crude cellular or nuclear extracts. Nowhere does *Giordano* mention expressing epitope-tagged RBP/RAP in cells, much less partitioning the mRNA-protein complexes by capturing the endogenously expressed epitope-tagged protein onto a solid support. Searching *Giordano* for the words "tag" or "epitope," one may only find references to expressed sequence tag (EST) sequences in col. 12, lines 41-45. ESTs bear no relation to the claimed invention. Therefore, *Giordano*, does not disclose all elements of claim 48. Accordingly, the § 102 rejection of claim 48 and its dependent claims should be withdrawn.

For at least the reasons stated above, Applicants believe that all claims are now in condition for allowance. Applicants request that the Examiner enter the proposed amendments, reconsider outstanding rejections and expediently allow all pending claims. The Examiner is invited to call the undersigned with any questions or concerns.

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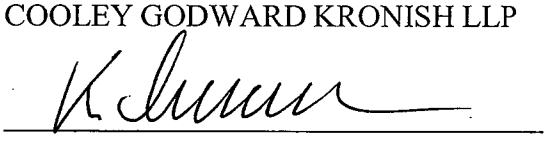
Respectfully submitted,
COOLEY GODWARD KRONISH LLP

By: 

Konstantin M. Linnik, Ph.D.
Attorney for Applicant(s)/Assignee(s)
Reg. No. 56,309
Tel.: (617) 937-2340
Email: klinnik@cooley.com

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